## REMARKS/ARGUMENTS

### 1. Claim Status and Support

Amended claim 40 and claims 41-43 are currently pending. Support for the amendments can be found in the specification as originally filed. Support for the amendment to claim 40 can be found *inter alia* on page 71, line 20 through page 72, line 11 (Example 7). Support for new claims 44-47 can be found *inter alia* on page 14, line 20 through page 15, line 19. Support for new claim 48 can be found *inter alia* on page 49, line 21 through page 60, line 4 (Example 3) and Example 7. No new matter is added as a result of these amendments.

### 2. Rejections under 35 USC § 103(a)

**A.** Claims 40-42 are rejected under 35 U.S.C. 103(a) as being unpatentable over Marks et al. in view of Proffitt et al.

In order to establish a *prima facie* case of obviousness the prior art references alone or in combination must teach or suggest ***all*** the claim limitations. [emphasis added] MPEP § 706.02(j).

As an initial matter the Patent Office has, for the second consecutive office action, mischaracterized the Applicants' arguments in the response filed June 8, 2007 and has asserted that Applicants admitted that Marks teaches co-localization of antibody or bacteriophage with its receptor upon internalization. In fact, this is the exact opposite of what the Applicants stated in the June 8, 2007 response. Applicants stated the following:

> Marks teaches labeling of antibodies or bacteriophage (which are **not** cell surface receptors) and assessing **internalization of antibodies or bacteriophage** by fluorescent microscopy. Contrary to the Patent Office's characterization, the disclosure of Marks at column 13, lines 44-55 does **not** teach methods for identifying **internalizing receptors**. (Page 5, bottom of page, response filed June 8, 2007).

Thus, Applicants have consistently argued that Marks does not teach any methods for identifying, much less measuring, receptor internalization.

Pending claim 40 recites the following:

> A machine readable storage medium comprising a program containing a set of instructions for causing a cell screening system to execute **procedures**

**for measuring internalization of cell surface receptor proteins in individual cells** on an array of locations which contain multiple cells, wherein the procedures comprise:

a) identifying internalized cell surface receptor proteins in multiple individual cells on the array of locations, wherein the individual cells comprise at least a first luminescent reporter molecule that **labels a cell surface receptor protein of interest to produce a labeled cell surface receptor protein**, and at least a second luminescent reporter molecule that reports on cells, wherein the identifying comprises determining whether luminescent signals from the **labeled cell surface receptor protein** in the individual cells identified by the at least second luminescent reporter molecule meet or surpass a user-defined threshold luminescent intensity, wherein luminescent signals from the **labeled cell surface receptor protein** that meet or surpass the user-defined threshold luminescent intensity represent an internalized cell surface receptor protein;

b) calculating a number and/or percent of the **individual cells that internalized the labeled cell surface receptor protein** wherein the calculations provide a measure of internalization of the cell surface receptor protein in the individual cells; and

c) **displaying data on the measure of internalization of the cell surface receptor protein in the individual cells**.

The Patent Office asserted that the "claims only require[s] [that] that the first luminescent reporter molecule report on a cell surface receptor protein of interest." While the Applicants traverse the Patent Office's assertion, claim 40 has been amended to make it clear that luminescent signals from the **labeled cell surface receptor protein in the individual cells** are assessed for meeting or surpassing a user-defined threshold and thus to represent an internalized cell surface receptor protein, and then calculating a number and/or percent of individual cells that internalized the labeled cell surface receptor protein, as a measure of internalization of cell surface receptor proteins in the individual cells.

In contrast Marks teaches labeling of antibodies or bacteriophage and assessing internalization of the labeled antibodies or bacteriophage by fluorescent microscopy. Thus, Marks does not teach, suggest or make obvious labeling the cell surface receptor protein. As such, it cannot teach determining whether luminescent signals from the labeled cell surface receptor protein in the individual cells meet or surpass a user-defined threshold luminescent intensity, wherein luminescent signals from the labeled cell surface receptor protein that meet or surpass the user-defined threshold luminescent intensity represent an internalized cell surface receptor protein.

Nor does Marks, as admitted by the Patent Office in paragraph 11 (page 5) of the instant Action, teach calculating the number and or percent of individual cells that internalized the labeled cell surface receptor protein, nor of displaying such data. Thus Marks does not teach, suggest, or make obvious all, or even most, of the limitations recited in pending claim 40.

The Patent Office further cites Proffitt in combination with Marks and asserts that Proffitt "teaches a computerized system cells screening system and algorithm that is able to measure the relative cell numbers that contain a fluorescent label." (paragraph 12, instant action and abstract of Proffitt). As stated by the Patent Office, Proffitt teaches that the "total relative fluorescence intensity for the entire well containing the cells is determined." (abstract) In contrast, the pending claims recite "calculating a number and/or percent of the **individual cells** that internalized the labeled cell surface receptor protein wherein the calculations provide a measure of internalization of the cell surface receptor protein in the **individual cells**." Thus, Proffitt does not teach, suggest, or make obvious **any type of** measurements from **individual cells** as recited in the pending claims, but rather teaches measuring the "total relative fluorescence intensity for the entire well containing the cells." As such, it cannot teach determining whether luminescent signals from the labeled cell surface receptor protein in the individual cells meet or surpass a user-defined threshold luminescent intensity, wherein luminescent signals from the labeled cell surface receptor protein that meet or surpass the user-defined threshold luminescent intensity represent an internalized cell surface receptor protein. Nor does Proffitt teach, suggest, or make obvious calculating the number and or percent of individual cells that internalized the labeled cell surface receptor protein, nor of displaying such data. .

Thus, the combination of Marks and Proffitt does not cure the deficiencies of Marks identified above with respect to claim 40 or its dependent claims. Therefore, Applicants respectfully request reconsideration and withdrawal of the rejection.

**B.** Claim 43 is rejected under 35 U.S.C. 103(a) as being unpatentable over Marks et al. in view of Proffitt et al. as applied to claim 40-42 above, and further in view of Dunlay et al.

In order to establish a *prima facie* case of obviousness the prior art references alone or in combination must teach or suggest ***all*** the claim limitations. [emphasis added] MPEP § 706.02(j).

As argued above, Marks in combination with Proffitt do not teach, suggest or make obvious all of the claim limitations of claims 40-42. The combination of Dunlay with Marks and Proffitt does not cure these deficiencies. Thus, the combination of referenced do not teach, suggest or make obvious independent claim 40 or dependent claims 41-43 which share the limitations of claim 40. Therefore, Applicants respectfully request reconsideration and withdrawal of the rejection.

## 3. Conclusion

Based on all of the above, the Applicants believe the claims are now allowable. If there are any questions or comments regarding this response, the Patent office is encouraged to contact the undersigned attorney as indicated below.

Respectfully submitted,

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